

WHAT IS CLAIMED:

546 07

1. A method of testing the immune compatibility of cloned cells or tissues in an animal model, comprising:
 - 5 a. obtaining a cell from a donor animal;
 - b. transferring the nucleus from said cell into a recipient oocyte or other suitable recipient cell to generate an embryo;
 - c. isolating an embryo having at least one cell, an embryonic disc and/or stem cell from said embryo;
 - 10 d. injecting said embryo, disc and/or stem cell into said donor animal at the same time as control embryonic disc and/or stem cell; and
 - e. examining the injection sites for teratoma formation.
2. The method of Claim 1, wherein said cell from said donor animal is transfected with a heterologous gene prior to nuclear transfer.
- 15 3. The method of Claim 1, wherein said donor and control embryonic discs and/or stem cells are injected subcutaneously or into the paralumbar fascia.
4. The method of Claim 1, wherein said teratoma, if formed, is removed and examined for the presence of germ layers.
- 20 5. The method of Claim 4, wherein the germ layers, if formed, are separated for the purpose of detecting or isolating specific cell types.

6. The method of Claim 1, wherein the cell obtained from said donor animal is a fibroblast.

7. The method of Claim 2, wherein said heterologous gene is a reporter gene selected from the group consisting of green fluorescent protein (GFP), beta-5 galactosidase, and luciferase.

8. The method of Claim 2, wherein said heterologous gene encodes a protein that is secreted.

9. The method of Claim 8, wherein said protein generates an immune response.

10. The method of Claim 8, wherein said protein is a therapeutic protein.

11. The method of Claim 5, wherein the germ layer cells are further used in assays to evaluate potential developmental signals that control cell differentiation.

12. The method of Claim 5, wherein at least one type of cell found in the germ layers is used to engineer a tissue.

15. The method of Claim 12, wherein said engineered tissue is transplanted back into said donor animal to test immune compatibility.

14. The method of Claim 12, wherein said engineered tissue is selected from the group consisting of smooth muscle, skeletal muscle, cardiac muscle, skin, kidney and nervous tissue.

20. 15. A method of generating immune compatible tissues for transplantation, comprising:

5

- a. obtaining a donor cell from an intended transplant recipient;
- b. transferring the nucleus from said cell into a recipient oocyte or other suitable recipient cell to generate an embryo or fetus;
- c. isolating from the embryo or fetus a cell of the type required for transplantation; and
- d. engineering a tissue from said cells.

16. The method of Claim 15, comprising the following additional steps between said steps (c) and (d):

10

- i. isolating an embryonic disc and/or stem cell from said embryo;
- ii. injecting said disc and/or stem cell into an immune compromised animal;
- iii. isolating the resulting teratoma;
- 15 iv. isolating from the teratoma a cell of the type required for transplantation; wherein said teratoma cell is used to engineer said immune compatible tissue.

20 17. The method of Claim 15, wherein said tissue contains cells comprised of isogenic nuclear DNA and allogeneic mitochondrial DNA.

18. The method of Claim 15, wherein said tissue contains cells comprised of isogenic nuclear DNA and a mixture of allogeneic and isogenic mitochondrial DNA.

19. The method of Claim 15, wherein said tissue is selected from the group consisting of smooth muscle, skeletal muscle, cardiac muscle, skin, kidney and nervous tissue.

20. A method of providing a patient in need of a transplant with an immune-compatible transplant, comprising:

- a. obtaining a donor cell from said patient;
- b. transferring the nucleus from said cell into a recipient oocyte or other suitable recipient cell to generate an embryo;
- c. isolating an embryonic disc and/or stem cell from said embryo;
- 10 d. injecting said disc and/or stem cell into an immune compromised animal in order to form a teratoma;
- e. isolating the resulting teratoma;
- f. isolating a cell of the type required for transplantation from the teratoma;
- 15 g. engineering a tissue from said cells; and
- h. transplanting said engineered tissue into said patient.

21. The method of Claim 20, wherein said immune compromised animal is a skid or nude mouse.

20 22. The method of Claim 20, wherein the donor cell obtained from said intended transplant recipient is a fibroblast.

23. The method of Claim 20, wherein said engineered tissue is selected from the group consisting of smooth muscle, skeletal muscle, cardiac muscle, skin, kidney and nervous tissue.

24. The method of Claim 20, wherein said engineered tissue comprises 5 cells having isogenic nuclear DNA and allogeneic mitochondrial DNA.

25. The tissue engineered by the method of Claim 20.

26. An isolated tissue generated by the method of Claim 20.

27. The method of Claim 1, wherein said animal is an ungulate.

28. The method of Claim 27, wherein said ungulate is a bovine.

10 29. The method of Claim 15, wherein said animal is an ungulate.

30. The method of Claim 29, wherein said ungulate is a bovine.

31. The method of Claim 16, wherein said animal is an ungulate.

32. The method of Claim 31, wherein said ungulate is a bovine.

15 33. The method of Claim 20, wherein said intended transplant recipient is a human.

34. The method of Claim 16, wherein said patient is a human.

35. The method of Claim 16, wherein said donor cell is genetically altered prior to nuclear transfer.

36. The method of Claim 35, wherein said genetic alteration comprises the transfection of at least one heterologous gene.

37. The method of Claim 35, wherein said genetic alteration comprises the disruption of at least one native gene.

sub a 5 38. An animal containing at least one teratoma produced from a cloned cell.

39. The animal of Claim 38, wherein said animal is an ungulate.

40. The animal of Claim 39, wherein said ungulate is a bovine.

10 41. The animal of Claim 38, wherein said at least one teratoma is located in the paralumbar fascia.

42. The animal of Claim 38, wherein said teratoma is not rejected by the animal's immune system.

43. The animal of Claim 42, wherein said teratoma comprises cloned cells having isogenic nuclear DNA and allogeneic mitochondrial DNA.

15 44. A teratoma isolated from the animal of Claim 38.

45. The teratoma of Claim 44, wherein the teratoma contains cells from all three germ layers.

46. The teratoma of Claim 44, wherein said teratoma is derived from a cloned ungulate cell.

47. The teratoma of Claim 46, wherein said teratoma is derived from a cloned bovine cell.

Sub Q9 48. The teratoma of Claim 48, wherein said teratoma comprises ~~cloned~~ cells having isogenic nuclear DNA and ~~allogeneic~~ mitochondrial DNA, or a mixture 5 of ~~allogeneic~~ and isogenic mitochondrial DNA.

49. A stable graft comprised of isogenic nuclear DNA and ~~allogeneic~~ mitochondrial DNA.

50. The graft of Claim 49, wherein the cells of said graft are made by nuclear transfer of an isogenic somatic cell into an allogeneic recipient cell.

10 51. The graft of Claim 49, wherein said tissue is selected from the group consisting of kidney, cardiac muscle and skeletal muscle.

52. A method of identifying mitochondrial histocompatibility antigens using cross-species nuclear transfer, comprising:

- a. obtaining cells from a donor mammal;
- b. transferring nuclei from said donor mammal into at least two recipient oocytes or other suitable recipient cells of a mammalian species other than said nuclear donor to generate embryos, wherein said at least two recipient cells are allogeneic with regard to mitochondrial DNA;
- c. isolating an embryo having at least one cell, an embryonic disc 20 and/or stem cell from said embryo;
- d. injecting said embryo, disc and/or stem cells separately back into said donor mammal as to generate a specific panel of antibodies and/or lymphocytes; and
- e. comparing panels of antibodies and/or lymphocytes generated 25 in response to said allogeneic mitochondrial backgrounds in order to identify

mitochondrial antigens and/or epitopes that are recognized by the immune system of said donor mammal.

53. The method of claim 52, wherein said embryo, disc and/or stem cells
5 are injected into separate mammals which are isogenic to the nuclear donor with
respect to both nuclear and mitochondrial DNA.

54. Antibodies specific for the mitochondrial antigens identified in the method of Claim 52.

55. Lymphocytes specific for the mitochondrial antigens identified in the
10 method of Claim 52.